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# US ARMY MEDICAL RESEARCH LABORATORY

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REPORT NO. 732

## THRESHOLD LESIONS INDUCED IN PORCINE SKIN BY $CO_2$ LASER RADIATION

Interim Report

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Arnold S. Brownell, Ph. D.
Wordie H. Parr, Ph. D.
Captain David K. Hysell, VC
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Captain Robert S. Dedrick, VC

7 June 1967

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7 June 1967

Cutaneous and Deep Burns Induced by Laser Radiation
Work Unit No. 103
Surgery
Task No. 01
Research in Biomedical Sciences
DA Project No. 3A014501B71R

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USAMRL Report No. 732
DA Project No. 3A014501B71R


## ABSTRACT

### THRESHOLD LESIONS INDUCED IN PORCINE SKIN BY $CO_2$ LASER RADIATION

### OBJECTIVE

To determine the exposure conditions necessary to produce threshold thermal lesions in porcine skin by $CO_2$ laser radiant energy of 10.6 micron wavelength over a wide range of exposure times and power densities.

### METHODS

The skin of white pigs was exposed to $CO_2$ laser radiation with varying combinations of power density and exposure time.

### RESULTS AND CONCLUSIONS

The dose-response relationship for threshold burns has been determined for power densities within the range of 1 to 8 watts/cm$^2$ and exposure times 0.4 to 18 seconds. In the range from 1.5 to 8 watts/cm$^2$ the data fit the equation $H = 4.13t^{-.607}$ where H = incident power density (watts/cm$^2$) and t = median effective exposure time (sec). Limited data suggest that below 1.5 watts/cm$^2$ this relationship changes. The data provide information for establishing safety standards for $CO_2$ laser radiation.

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## THRESHOLD LESIONS INDUCED IN PORCINE SKIN BY $CO_2$ LASER RADIATION

### INTRODUCTION

The rapid development of lasers and the increasing use of these instruments in military applications necessitates the evaluation of potential hazards associated with their use. One area of potential hazard is in the induction of cutaneous burns by laser radiant energy. Extensive studies have been carried out on the production of cutaneous burns by non-coherent radiant energy with a wide wavelength distribution in the visible and near-infrared regions of the spectrum (1-4). The extrapolation of these data to laser induced burns is difficult because (a) the analysis of these data as a function of wavelength is complex due to the marked variation in the optical properties of skin with wavelength, and (b) the relations established in these studies may not be applicable in the range of high power densities and short exposure times available with lasers.

The recent development of high power continuous wave (CW) $CO_2$ lasers with an output radiation of 10.6 microns adds a new impetus to the necessity for these studies. The high absorption coefficient of radiant energy of this wavelength in aqueous media plus the continuous wave operation makes it possible to deposit enormous amounts of energy in a very small volume of tissue. The potential hazards are quite evident but need to be clearly defined with respect to power density and exposure time. This study is for the purpose of defining the power density and exposure time to produce minimal detectable visible lesions in the skin.

### METHODS

The $CO_2$ laser was designed and constructed by the Martin Marietta Corporation, Orlando, Florida (5). The optical resonant cavity is 264 centimeters in length of which 220 cm is excited by a d.c. power supply providing 30 KV at 200 ma. The bore of the discharge tube is 4.5 cm. The output window is made of Irtran II coated for 20% transmission with an internal 50 meter radius of curvature. The other end of the discharge tube is sealed with a KCl Brewster angle window. External to the Brewster window is a gold coated quartz concave mirror with a 20 meter radius of curvature. Between the rear mirror and the Brewster window is a camera shutter operated by an electrical timing

device. The discharge tube walls are liquid cooled. The gas mixture (4% $CO_2$, 14% $N_2$, 82% He) is continuously replenished by a constant flow technique. For these experiments the power output was adjusted by varying the gas pressure and holding the discharge current constant at 50 ma. The beam size was limited by a 3/4 inch aperture.

The laser output was routinely measured with a double cone calorimeter (6). This was calibrated against a constant flow water calorimeter with a AgCl window (6). As an additional check, the double cone calorimeter was compared with a calibrated TRG calorimeter using a ruby laser as the energy source. These two calibration factors agreed within 4%. The relative energy flux distribution in the output beam was measured by a scanning device designed and built by Martin Marietta Corporation (7).

Yorkshire pigs, free of visible skin pigmentation, were used. Their weights ranged from 22 to 65 lb and averaged 37 lb. Acepromazine, 1 mg/lb, was given as a preanesthetic. The anesthetic agent, pentobarbital sodium (nembutal), was administered intravenously in an ear vein until the desired effects were achieved. The total anesthetic dose averaged 7.2 cc of a 60 mg/cc solution of the pentobarbital sodium. Electric animal clippers with a No. 40 blade were used to remove the hair from one side of each animal. The use of an electric razor to shave the test area was discontinued early in the study because of occasional irritation to the skin.

On the prepared side of each animal an area of the skin was divided into four rows and ten columns, providing a grid of 40 squares. The placement of the grid and the burns are shown in Figure 3 (page 7). Three to eight animals were irradiated at each power density used. Each exposure time-power density combination was replicated twelve to twenty times. Each animal within a series received, as nearly as possible, the same number of exposure combinations. The exposure times were randomly assigned to the grid in order to minimize area to area variations in sensitivity. The room temperature was held within 72-78°F in order to reduce the influence of ambient temperature (8).

The burns were evaluated independently by two investigators 18 to 24 hours after exposure. Discrepancies were reevaluated. For the purpose of this investigation, the evaluation was as follows: 0 - no change visually detectable, + - detectable erythema.

The data were graphically analyzed by the probit method of Litchfield and Wilcoxon (9).

## RESULTS AND DISCUSSION

In order to achieve the power densities required over a reasonably large area it was necessary to adjust the laser for highly multimoded operation. Under these conditions the beam pattern is an array of filaments within the beam, each filament having a rather sharply peaked energy flux distribution. With the proper alignment of the mirrors, these filaments have a fairly even spatial distribution throughout the beam cross section, the inter-filament separation being between 1 and 2 mm. Prior to each experiment the beam pattern was evaluated by graded exposures to Thermofax paper.

Figure 1 demonstrates the relative energy flux distribution in the laser beam as measured by the scanning device. The relative power

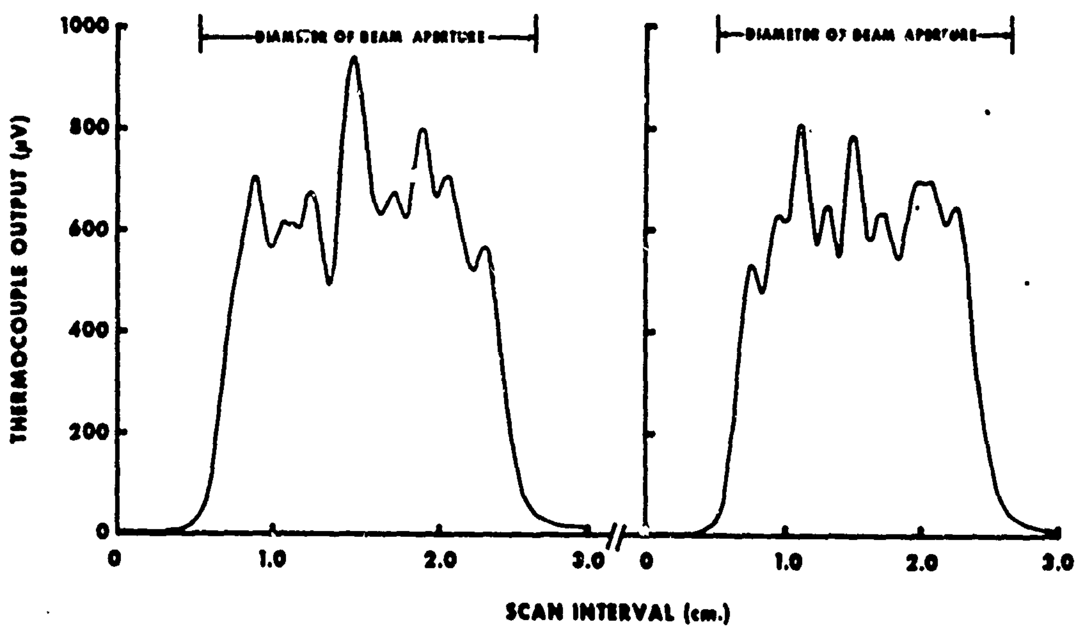


Fig. 1. Relative energy flux distribution across $CO_2$ laser beam.

density is indicated by the measured detecting thermocouple output. Each graph represents the relative power distribution in a scan line, somewhat less than 1 mm in diameter, across the center of the beam. The two measurements were made a few minutes apart without changing either the operating conditions of the laser or the position of the scanning device. The rate of scan was 9.2 mm/min in one direction, and 8.0 mm/min in the reverse direction. The variation in intensity of

each filament with time is quite evident. However, the time variation is of a low order usually requiring a few minutes to change significantly. As best as can be determined, the spatial distribution of individual filaments changes little, if any. Tracings such as shown can be regarded only as representing less than the maximum variation in the spatial distribution of the beam intensity because of the limit of cross sectional resolution of the scanning device, the low probability of the scan line traversing the exact center of each filament, and the inherent time variation of the peak power in each filament. The response of Thermofax paper to graded exposures to the beam suggests that the spatial power distribution is not very different from that represented here. A reasonable estimate is that the average maximum and minimum intensity is less than 25% above or below the mean intensity.

The dose-response data for 700 burns are presented in Table 1 (next page). The number of burns in each grading classification is tabulated with respect to power density and exposure time. The calculated median effective exposure time ($EEt_{50}$) and median effective dose ($ED_{50}$) for each power density is also given. The $EEt_{50}$ and $ED_{50}$ are the exposure time and energy density, respectively, at each power density that has a 50% probability of producing a detectable lesion.

The relationship between the power density and the median effective exposure time is graphically demonstrated by the double logarithmic plot in Figure 2 (page 6). The 95% confidence limits of the exposure times are indicated by bars.

Within the range of power densities from 1.7 to 8.0 watts/cm$^2$ and exposures from 0.3 to 5 sec the points approximate a straight line. This straight line portion of the curve as determined by the method of least squares fits the equation:

$$H = 4.13t^{-.607}$$

where H = incident power density (watts/cm$^2$)
t = median effective exposure time (sec).

The calculated 95% confidence limits of the [illegible]ctor for t are .598 - .616.

It may be argued that the entire plotted range can be fitted reasonably well by a straight line function. However, because of a better

TABLE 1

Tabulated Dose Response Data

| Power Density (watts/cm²) | Exposure Time (sec) | No. of Burns 0 | No. of Burns + | No. of Burns Total | EEt50 (sec) | ED50 (cal/cm²) |
|---|---|---|---|---|---|---|
| 7.7 | .39 | 5 | 6 | 11 | .37 (.32 - .43) | .68 (.60 - .78) |
| | .49 | 4 | 18 | 22 | | |
| | .59 | 0 | 22 | 22 | | |
| | .68 | 0 | 22 | 22 | | |
| 4.8 | .60 | 10 | 2 | 12 | .71 (.65 - .77) | .82 (.75 - .88) |
| | .69 | 8 | 4 | 12 | | |
| | .79 | 2 | 7 | 9 | | |
| | .90 | 0 | 11 | 11 | | |
| | 1.10 | 0 | 11 | 11 | | |
| 3.7 | .60 | 12 | 0 | 12 | 1.32 (1.14 - 1.53) | 1.19 (1.02 - 1.38) |
| | .69 | 12 | 0 | 12 | | |
| | .79 | 16 | 2 | 18 | | |
| | .89 | 18 | 0 | 18 | | |
| | .99 | 17 | 2 | 19 | | |
| | 1.20 | 11 | 1 | 12 | | |
| | 1.40 | 7 | 12 | 19 | | |
| | 1.60 | 2 | 16 | 18 | | |
| | 1.80 | 1 | 19 | 20 | | |
| | 2.00 | 0 | 19 | 19 | | |
| | 2.20 | 1 | 19 | 20 | | |
| | 2.41 | 0 | 19 | 19 | | |
| | 2.61 | 0 | 19 | 19 | | |
| 2.6 | 1.40 | 12 | 0 | 12 | 2.26 (2.12 - 2.41) | 1.38 (1.29 - 1.48) |
| | 1.70 | 18 | 0 | 18 | | |
| | 2.00 | 16 | 2 | 18 | | |
| | 2.31 | 8 | 10 | 18 | | |
| | 2.61 | 1 | 17 | 18 | | |
| | 2.91 | 2 | 16 | 18 | | |
| | 3.22 | 0 | 16 | 16 | | |
| | 3.53 | 0 | 18 | 18 | | |
| 1.7 | 3.93 | 12 | 5 | 17 | 4.15 (3.82 - 4.50) | 1.68 (1.55 - 1.82) |
| | 4.23 | 6 | 15 | 21 | | |
| | 4.55 | 4 | 17 | 21 | | |
| | 4.84 | 5 | 16 | 21 | | |
| | 5.24 | 0 | 18 | 18 | | |
| | 5.64 | 0 | 19 | 19 | | |
| 1.1 | 8.03 | 15 | 0 | 15 | 13.1 (12.5 - 13.8) | 3.35 (3.20 - 3.52) |
| | 10.1 | 15 | 0 | 15 | | |
| | 12.0 | 12 | 3 | 15 | | |
| | 14.0 | 3 | 12 | 15 | | |
| | 16.0 | 0 | 15 | 15 | | |
| | 18.0 | 0 | 15 | 15 | | |

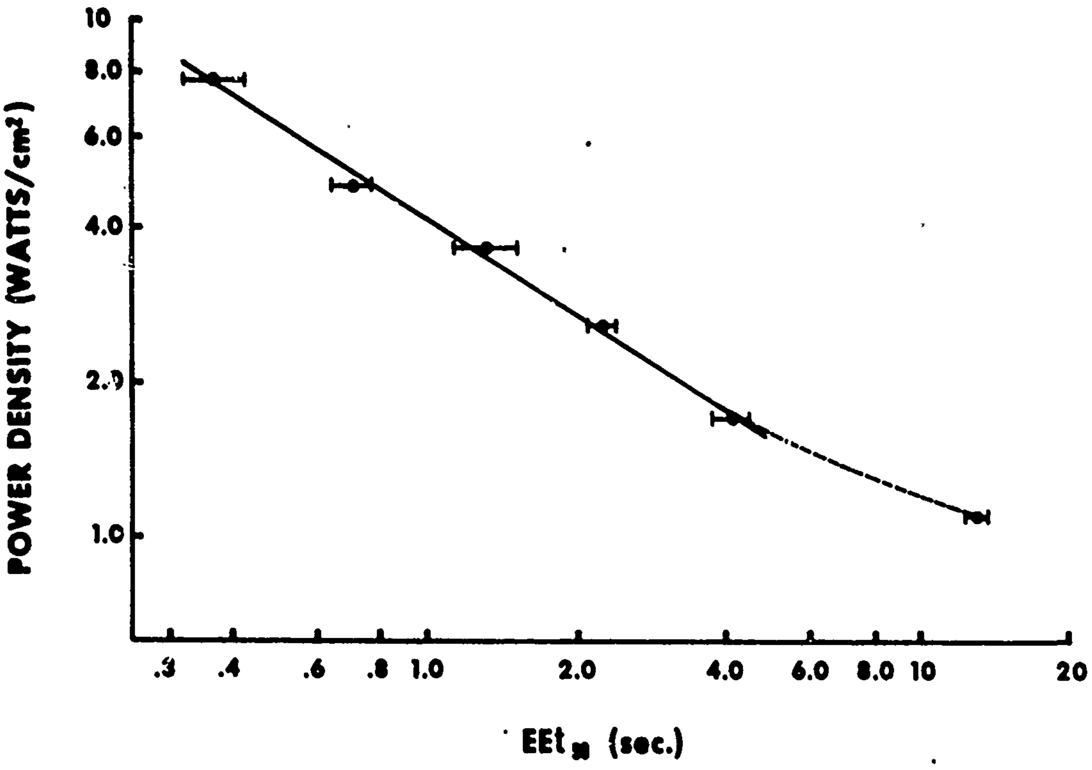


Fig. 2. Median effective exposure time vs. power density for threshold burns.

fit as shown and because preliminary data on more severe burns also show a change in slope in this exposure range, it is felt that the plot as presented is a more realistic evaluation of the data. More measurements at lower power densities are needed to determine the slope of the curve in this range.

Fine et al (10) found in the case of immediate white burns in mouse skin following exposure to $CO_2$ laser radiation within the range of 0.5 to 5 sec exposure time that the dose effect relationship was best described by the power density varying inversely with the square root of the time. They concluded from this that the opaque, homogeneous model evaluated at the surface for tissue in this time range best fit their data. It may be that in the case of mouse skin, which is much thinner than pig skin, the lesions represent more of a surface phenomenon than do those of the porcine skin. The data presented in Figure 2 suggest that for exposure times in excess of 6 sec the opaque model may also adequately describe the dose effect relationship for porcine skin. For exposure times less than 6 sec the need for another model is desirable. Such a mathematical model should take into account the tissue depth appropriate to the measured response as well as the finite absorption coefficient of radiation with this wavelength.

It should be pointed out that a threshold burn as defined here does not represent the minimal observed effect following exposure. Invariably during the exposure period, the exposure site develops an erythema. In most cases this erythema spreads beyond the exposed area. Within a few minutes to a few hours this initial diffuse reddening decreases and in the milder burns disappears entirely. Only those skin sites showing a perceptible erythema 24 hours later are considered as positive burns.

The photograph in Figure 3 was taken a few minutes after the exposures were completed. Note the diffuse erythematous areas in the top row which was the last to be exposed. In the first row exposed, the bottom row, the lesions are clearly defined. Approximately 15 minutes lapsed between the exposures on the bottom and top rows. An example of an initial erythema that completely fades in 24 hours is illustrated in the upper right square.

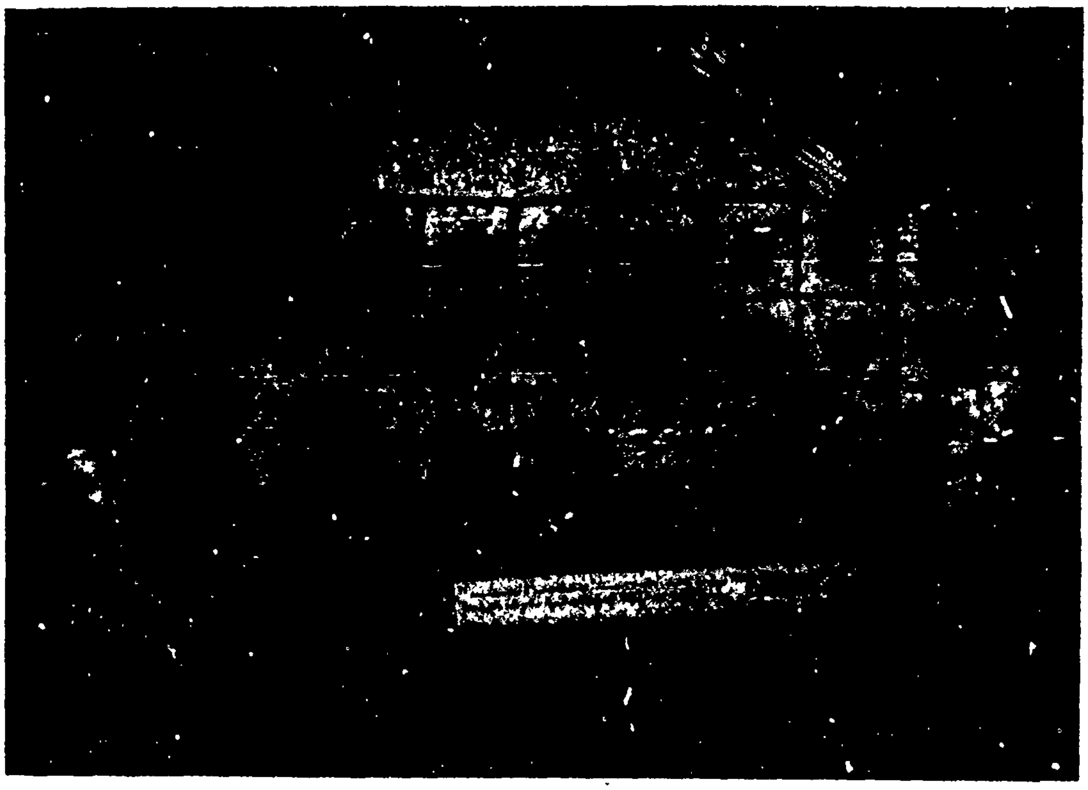

Fig. 3. Porcine skin immediately following exposure to laser radiation of 2.5 watts/$cm^2$ and exposure times of 1.4 to 5.2 sec.

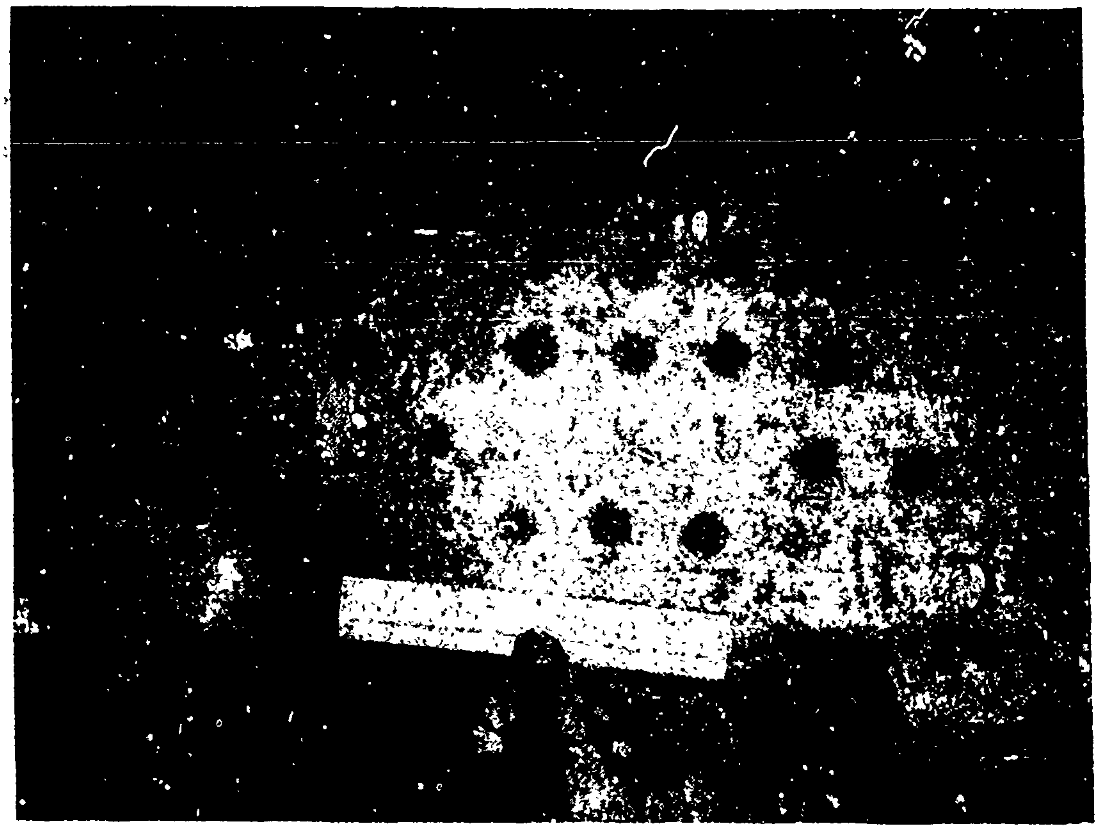

Fig. 4. Porcine skin 24 hours following exposure to laser radiation of 2.5 watts/cm$^2$ and exposure times of 1.4 to 5.2 sec.

## CONCLUSIONS

The equation $H = 4.13t^{-.607}$ describes the exposure conditions necessary to produce minimal gross lesions to porcine skin in the range of 1.5 to 8 watts/cm$^2$. Additional data are required to establish dose-response data outside this power density range.

The results provide additional information pertinent to establishing safety standards for $CO_2$ laser radiation. The suggested mathematical equation can adequately predict threshold burns over a limited range of power densities and exposure times. In addition, the data indicate a more sophisticated mathematical model is needed to predict the induction of threshold burns over a wider range of exposure conditions and provides basic data for its development.

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13. ABSTRACT


The skin of white pigs was exposed to $CO_2$ laser radiation with varying combinations of power density and exposure time. ~~(U)~~

The dose-response relationship for threshold burns has been determined for power densities within the range of 1 to 8 watts/$cm^2$ and exposure times 0.4 to 18 sec. In the range from 1.5 to 8 watts/$cm^2$ the data fit the equation $H = 4.13t^{-.607}$ where H = incident power density (watts/$cm^2$) and t = median effective exposure time (sec). Limited data suggest that below 1.5 watts/$cm^2$ this relationship changes. The data provide information for establishing safety standards for $CO_2$ laser radiation. (U)


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| Thermal | | | | | | |
| Skin | | | | | | |
| Burns | | | | | | |
| Infrared rays | | | | | | |